THE CEREBRAL AND OCULAR COMPLICATIONS OF ANÆMIA AND THE PROBABLE RELATIONSHIP OF THESE TO THROMBOSIS

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An Address

Delivered to the Medico-Chirurgical Society of Glasgow

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THE CEREBRAL AND OCULAR COMPLICATIONS OF ANÆMIA AND THE PROBABLE RELATIONSHIP OF THESE TO THROMBOSIS.

Mr. President and Gentlemen,

I have the honour to offer to the Society some observations on the cerebral and ocular complications which occur as occasional events in the clinical histories of anæmic women, and I propose to maintain, subject to your better judgment, that the interpretation of these events is to be found in the intravascular formation of blood clot. That among the special characters which pertain to the anæmic state there must be included an undue tendency to blood coagulation is generally admitted. At least, this is true so long as the blood is contained within the blood-vessels. When withdrawn from the vessels it would appear that the opposite condition obtains and that clotting is both delayed and incomplete. Upon what exactly this difference depends it may be difficult to say, but the fact certainly suggests that intravascular coagulation in anæmia is dependent less on some particular quality of the blood than on an abnormal state of the circulation; and seeing that such clotting is far more frequent in venous than in arterial channels, and that it is mainly confined to situations where, for anatomical reasons, the movement of the blood is comparatively slow, the suggestion may be accepted that an important or determining factor in the thromboses of anæmia is a delayed or sluggish rate of blood-flow. There are, however, quite a number of rival theoretical explanations of the occasional occurrence of thrombosis in anæmic patients, but none of them would appear to have secured anything like unanimous acceptance. In connection with this communication it is not necessary that these explanations should be discussed; nor is it necessary to enquire why, although thrombosis is in exceptional instances a prominent feature in anæmia, the enormous majority of the cases of this condition give no clinical evidence of any such tendency. For the most part indeed the disease, at least as seen in the shape or fashion of chlorosis, pursues a course so uniform and so undisturbed that even a considerable clinical experience may fail to secure a personal introduction to any development which owes its existence to thrombotic or other

exceptional events. Yet it is beyond dispute that serious and even fatal complications sometimes occur in anæmie women, and it is not less certain that the explanation of these is to be found in intravascular clot formation. Hence, whatever be the exact pathological interpretation of this event or of its restriction to a relatively small number of patients, it is necessary to accept thrombosis as an occasional accident in the course of anæmia and to be prepared, both as an exercise in diagnosis and as a practical responsibility in regard to treatment, to deal with the situations thus created. One of the objects of this communication is to suggest that not only certain acute and serious complications but also a number of comparatively minor disturbances occasionally observed in anæmie women owe their origin to intravascular blood-clotting. Such disturbances are perhaps more frequent than is generally allowed, and if the proposition that they are due to thrombosis is established they become of considerable clinical importance. For they then appear as warnings or danger signals of the possibility, or even of the probability, of clot formation on a large scale or in particularly dangerous situations, and they thus claim the special therapeutic measures by which results so disastrous may be averted.

In short, the argument here to be presented will be, that in thrombosis may be found an explanation not only of various grave, urgent, and well-recognised complications of the anæmic state, but also of certain relatively minor disturbances which appear as occasional departures from the usual course of anæmia as this exists in its simpler and less serious types.

Probably the most frequent and obvious exhibition of thrombosis in anæmia is met with in the large veins of the lower limbs. The symptoms include pain, tenderness, and œdema, and there may or may not be febrile temperatures. The thrombosis may extend from the femoral to the iliac veins, and even to the inferior vena cava; and in occasional instances it would appear that the process has been limited to these larger channels. It is rare for the veins of the upper limbs to be involved, but they are not wholly exempt; and the same is true of the large veins of the neck and chest. Of course, in all such cases there is a risk of pulmonary embolism, and the whole of the facts in this connection have been repeatedly verified by *post-mortem* examination. Apart from embolism, however, the prognosis in anæmie venous thrombosis is far from gloomy, and it is of interest to note that the circulation in the obstructed veins may be completely restored.

This is shown, not only by the disappearance of dropsy, but also by the recession of a collateral circulation, which, as a compensatory process, may have become established in superficial venous channels. Hence it must be accepted—and the fact is important in connection with the argument here to be advanced—that an obstructing clot formed in a vein in association with anæmia, may, presumably by absorption or organisation, be so completely removed as to cease to exercise any disturbing effect on the normal flow and movement of the circulation. Such a satisfactory issue has been observed even when the thrombotic process has been so widely spread as to affect the majority of the large veins both of the trunk and limbs.

The next situation to be recalled in connection with the occurrence of anæmic thrombosis is the intracranial veins and sinuses. Every now and then there is recorded in the medical journals the sudden development of acute cerebral symptoms in a young woman who, save for the existence of anæmia, had previously been regarded as entirely free from evidences of organic disease. The symptoms include severe headache, vomiting, pain in the neck, retraction of the head, stupor, delirium, various paralyses, and sometimes double optic neuritis, and in not a few of the cases there has been a fatal issue. In view of these symptoms, the diagnosis of intracranial tumour, or, when, as is sometimes the case, there are febrile temperatures, of meningitis, can hardly excite surprise. Yet there can be no doubt that most, if not all, of these cases are examples of venous thrombosis within the skull. This position is fully justified by the fact that in not a few instances *post-mortem* examination has demonstrated the presence of thrombosis in the intracranial veins and sinuses, and has at the same time failed to detect any other lesion capable of explaining either the symptoms or the fatal issue. There are other records in which, with similar symptoms, recovery has followed, and here the diagnosis of intracranial thrombosis has sometimes been supported by the development of thromboses in other situations, as, for example, in the jugular or femoral veins.

Upon this order of cases two observations may be offered. The first is, that as in thrombosis affecting the veins of the limbs both the obstructing clot and the consequences which attend such obstruction may, in a clinical sense, entirely disappear, the fact of complete recovery from an acute cerebral attack is not necessarily in conflict with a diagnosis of intracranial thrombosis as the cause of such an attack. If the

circulation may be restored after thrombosis of, say, the femoral vein, a similar result may surely follow thrombosis of the cerebral veins and sinuses. Thus, while widespread clot formation in this latter situation may perhaps produce a fatal result, a less extensive thrombosis may well be attended by clinical disturbances from which a complete recovery is possible. Hence, recovery, whether from a group of symptoms or perchance from a single symptom of manifestly cerebral origin, is entirely consistent with a diagnosis of thrombosis affecting the intracranial veins and sinuses.

The second remark submitted in connection with severe or fatal cerebral attacks occurring in anæmic women is that such cases may include among their symptoms the presence of double optic neuritis. If, therefore, these cases are due to thrombosis in the venous channels of the skull—and escape from this conclusion seems impossible—it follows that such thrombosis is an efficient cause of double optic neuritis. It is true that in some of the cases to which reference is now made optic neuritis has not been present. But these negative experiences cannot invalidate the definite and positive observations in which optic neuritis, existing together with other cerebral symptoms, has been found to have no pathological explanation other than intracranial thrombosis. The position finds an exact parallel in intracranial tumour. In some cases of tumour double optic neuritis is a prominent feature; in others the optic discs are normal. No one will use this latter fact as an argument to contest the proposition that intracranial tumour is competent as a cause of double optic neuritis. And the same conclusion must be applied to intracranial venous thrombosis. Among its possible effects, therefore, must be accepted the development of double optic neuritis.

It is hardly necessary to argue that another consequence may be a limited paralysis—say, for example, of one or other of the ocular muscles. If hemiplegia may be due to intracranial venous thrombosis—and this is beyond dispute—an ocular paralysis may well own a similar explanation, and indeed, there are many cases in which this association has been clearly established. Therefore it may be affirmed (1) that intracranial sinus and venous thromboses are the cause of the more or less severe cerebral attacks which occasionally complicate the course of chlorosis; and (2) that such thromboses may include among their consequences both double optic neuritis and ocular or other limited palsies.

With these propositions admitted, attention may be directed to the following summarised case-record :—

Maud E.,[1] aged 17 years, manifestly the subject of chlorosis, came to hospital complaining of double vision. Examination showed that the diplopia was due to paralysis of the right external rectus muscle, and that each optic disc was swollen and its edges concealed by exudation; there was also some retinitis. No albuminuria or evidences of organic disease other than the above were present. In the course of three months the patient had made a complete recovery.

Here, then, is a patient whose illness conforms strictly to the usual course of chlorosis, except for the fact that she has double optic neuritis and an ocular paralysis. These two events, if the argument already advanced is sound, may certainly be accounted for by intracranial thrombosis, to which, from her anæmic condition, the patient is undoubtedly liable. An alternative explanation is hard to suggest, and in view of all the circumstances the diagnosis of intracranial thrombosis may reasonably be held to be probable or even inevitable. Take a second case-record :—

Mary J.,[2] aged 22 years, admitted to hospital on account of severe headache, breathlessness, double vision, and failing sight. She was found to be the subject of chlorosis, of marked double optic neuritis with retinitis, and of paralysis of the left external rectus muscle. In addition, the knee-jerk could not be obtained on either side. The patient ultimately made a complete recovery, though the return of the knee-jerks was delayed for many months.

Here again the argument in reference to the cause of the optic neuritis and ocular paralysis may be repeated. Thrombosis will explain these facts, and it will also, presumably, explain the severe headache. Possibly the loss of the knee-jerks may not so readily accommodate itself to the diagnosis of intracranial thrombosis, but even here it may be remembered that certain intracranial tumours and also some forms of meningitis cause a similar loss. Further, in some of the more serious cases of anæmic thrombosis as proved by necropsy, distinct disturbance of the tendon-jerks has been observed, though this has perhaps been rather in the direction of excess than defect. Altogether there seems abundant justification for the claim that the above case is a further

[1] Reported in detail in *Glasgow Hospital Reports*, vol. ii, p. 142.

[2] See article by Mr. Ernest Clarke and Dr. Hawthorne, *Lancet*, 30th April, 1904, p. 1198.

example of double optic neuritis and an ocular paralysis occurring in a patient free from evidences of disease other than anæmia, and that these two symptoms must find in intracranial thrombosis their clinical and pathological explanation. Hence it would seem not only that double optic neuritis and an ocular paralysis may be numbered among the clinical events possibly attendant upon intracranial thrombosis, but also that they may appear as the only evidences of this condition. This conclusion brings such case-records as the two just quoted into a natural relationship with the more extreme examples of cerebral disturbance to which reference has already been made, and in a certain number of which intracranial thrombosis has been demonstrated on necropsy. The suggestion, in short, is that the difference between the two groups is merely one of degree, and that both groups own a common cause in the shape of thrombosis affecting the cerebral veins and sinuses.

This position is further strengthened by the fact that experiences intermediate between the two extremes are by no means wanting. There are well-authenticated cases of anæmia in which the patients have been attacked more or less suddenly by severe headache, pains in the neck, and vomiting, together with optic neuritis and ocular paralysis. It is common to suggest that the intracranial condition responsible for these symptoms is a localised and transient meningitis, or an œdema of the brain, though positive evidence in support of either of these views is difficult to find. On the other hand, thrombosis will cover all the facts, and, if allowed, will permit the construction of a graded series of cases, occurring in anæmic patients, characterised by more or less severe evidences of cerebral disturbance, and finding in intracranial blood-clotting a common bond of interpretation. At one extreme are fatal cases with such symptoms as coma, delirium, various paralyses, and sometimes, optic neuritis, and proved by necropsy to be dependent on intracranial thrombosis; next come examples of less severe but still considerable cerebral disturbances, including optic neuritis, and having a favourable termination, the diagnosis of intracranial thrombosis being confirmed by the occurrence of thromboses in the jugular, femoral, or other veins; succeeding these may be placed cases of unusually violent headache and vomiting, with optic neuritis and an ocular paralysis; and after these fall those cases of anæmia in which optic neuritis and an ocular paralysis are the sole unusual events. The earlier members of this series are demonstrably dependent on thrombosis, whilst, as

has already been argued, the cases in the last group readily adapt themselves to the same explanation. To detach the intermediate members of the series from the diagnosis of thrombosis is surely a somewhat arbitrary and unnatural proceeding, more especially when the alternative explanation suggested cannot possibly be more than a mere surmise. Hence the claim may be pressed, that in all the groups above presented as examples of more or less severe cerebral disturbances complicating anæmia there is one and the same underlying pathological condition—namely, thrombus formation in the intracranial veins or sinuses.

The question now arises whether the series of cases to be explained in this fashion can be carried a stage further. If optic neuritis and an ocular paralysis appearing together in a case of anæmia are to be attributed to intracranial thrombosis, is it not probable that when, under similar conditions, either exists alone, thrombosis is again the responsible cause? Thrombosis is competent to cause each of these events; it is also a recognised complication of the anæmic state; further, it may be questioned whether any more satisfactory, or indeed any equally satisfactory, explanation can be advanced. Hence thrombosis has a fair claim for recognition as the cause both of optic neuritis and of ocular paralysis when one or other of these symptoms appears as the sole unusual departure from the ordinary clinical course of simple anæmia. Ocular paralysis, it may be admitted, is only very occasionally in this position. Double optic neuritis, on the other hand, is a well-recognised complication of anæmia, and its occurrence has given rise to a good deal of speculation. Here it is presented—and the same may be said of an ocular paralysis—as the simplest clinical expression of an intracranial thrombosis, and the claim is made that an examination of the series of cases in which cerebral events complicate anæmia affords a presumptive proof of the correctness and adequacy of this proposition.

An attempt may now be made to find support for the argument that optic neuritis in anæmia is probably due to intracranial thrombosis by an examination of certain other conditions in which, without any very obvious explanation, optic neuritis occasionally appears. One of these is the acute anæmia following a free hæmorrhage, as from the stomach, intestine, or uterus. Standing alone, such cases have a very mysterious aspect. It will, however, be allowed that the condition of anæmia established by hæmorrhage is one in

which thrombosis may readily occur, as indeed is occasionally demonstrated by clot formation in the veins of the trunk or limbs after considerable loss of blood attending surgical operations. Hence it is not impossible—not even improbable—that free bleeding from a mucous surface may be followed by intracranial thrombosis, and such thrombosis may be advanced as the immediate cause of the optic neuritis in the cases now under consideration. It is at least suggestive that optic neuritis sometimes occurs in circumstances in which intracranial thrombosis is at least a possibility and where an explanation of the neuritis other than thrombosis is not easily imagined. Thus the occasional occurrence of optic neuritis in the acute anæmia following free hæmorrhages from mucous surfaces may be quoted in support of the doctrine that the optic neuritis sometimes seen in chlorosis is dependent on intracranial thrombosis.

Another condition in which optic neuritis may appear without any very manifest explanation is suppurative disease of the middle ear. In some of these cases the neuritis is associated with an ocular paralysis, and in others an ocular paralysis exists without any attendant optic neuritis. That is, purulent disease of the middle ear may present ocular complications identical with those occasionally found in simple anæmia—namely, optic neuritis and ocular paralysis—and these two events may be associated, or either of them may exist apart from the other. So far as optic neuritis is concerned the suggestion has been made that this may complicate tympanic disease altogether apart from intracranial complications. Obviously this can only mean apart from intracranial complications producing manifest cerebral symptoms, and the suggestion by no means guarantees the absence of sinus thrombosis, to which purulent otitis media is notoriously liable. For the most part, however, an optic neuritis, and perhaps still more an ocular paralysis, developing in the course of suppurative disease of the middle ear, means, without question, some more or less serious development within the skull. This development may be abscess, meningitis, or sinus thrombosis, and to judge from *post-mortem* records it would appear that of the three it is thrombosis which is most likely to give rise to optic neuritis.

Further, on more than one occasion it has happened that removal of clot from the lateral sinus has been followed by disappearance of an existing optic neuritis, and although in those cases where the patient has recovered it is impossible absolutely to exclude meningitis, the absence of evidences of

this condition has repeatedly been noted during the operation, and in some of the fatal cases necropsy has demonstrated that meningitis was not present, and that sinus thrombosis, perhaps with more or less œdema of the brain, was the only abnormal intracranial condition that could be detected. Still more, it has on several occasions been found that optic neuritis—and sometimes, too, an ocular paralysis—has existed in middle-ear disease quite apart from any other evidence of cerebral disturbance, and yet has disappeared, either without operation or after operative measures restricted to the mastoid and tympanum and not involving the cranial cavity. Obviously, in these cases, there cannot have been a cerebral abscess, and meningitis is improbable or at least is less probable than thrombosis. Among the recognised possibilities of the situation, therefore, there remains only thrombosis, and this, as shown in the records already quoted, is fully competent to explain the ocular conditions to which attention is now directed. In short, both optic neuritis and ocular paralysis may complicate middle-ear disease, and these complications may be explained by intracranial thrombosis, to which such disease may most certainly give rise. In certain fatal cases no intracranial condition competent to explain these events other than thrombosis has been discovered. Is it not, therefore, in the highest degree probable that when either optic neuritis or an ocular paralysis occurs as the single unusual event in the course of purulent disease of the middle ear that sinus or venous thrombosis is the responsible cause? And if this is true of middle-ear disease, is not a similar conclusion inevitable in reference to anæmia? In both diseases thrombosis is a possibility; in both, such thrombosis occasionally produces severe cerebral disturbances which may include either optic neuritis or an ocular paralysis; and in both, each of these last-mentioned facts may exist as the sole unusual event. To find, apart from thrombosis, an element common to the two diseases and able to account for optic neuritis or an ocular paralysis existing as an isolated fact is a task not easily accomplished, and it may therefore be urged that there is at least a strong presumption that intracranial thrombosis is in each instance the correct explanation.

Here then are three conditions, namely, acute anæmia, middle-ear disease, and chlorosis, in each of which optic neuritis apart from other complications occasionally makes its appearance. In each there is a possibility of intracranial thrombosis, and this must be allowed as at least a possible cause of the neuritis. To suggest some other cause, which is

at the same time common to the three diseases now in question, is a demand not readily satisfied. Hence it may be claimed that the study of the clinical history of acute anæmia and of purulent disease of the middle ear adds force to the contention that the optic neuritis sometimes seen in anæmic women is dependent on the occurrence of thrombosis in the veins and sinuses within the cavity of the skull.

From all these facts it might perhaps be concluded that the suggestion of intracranial thrombosis as the cause of the optic neuritis of anæmia is so strongly supported that it needs must command universal assent. This, however, is far from being the case. On the contrary, the proposal excites both incredulity and the opposition of rival interpretations. At the outset criticism applies to it this censure—that as there is no known or conceivable link by which thrombosis as a cause can be connected with optic neuritis as a consequence, the suggestion that the one is the cause of the other is not tenable. To this it may be answered that failure to provide an exact explanation of the mechanism uniting two associated events cannot be successfully pleaded against the proposition that one of these is the cause of the other provided there are, otherwise, valid reasons which render such a relationship probable. Were such a canon of criticism enforced it would, to quote but a single illustration, compel a refusal to accept intracranial tumour as a cause of optic neuritis, for the pathway leading from the one to the other is far from apparent. Yet, while claiming the protection of this general proposition, it may be advisable to attempt to find some apt and suggestive reasons on which a belief in the capacity of thrombosis to produce such consequences as optic neuritis and ocular paralysis may be reasonably based. Regarding the latter there can be no difficulty. Indeed, it is universally recognised that thrombosis in certain of the sinuses at the base of the skull does, as a matter of experience and presumably by pressure on the trunks of the cranial nerves, cause paralysis of the muscles of the eyeballs. Perhaps the most obvious examples of this condition are those in which the thrombosis involves the cavernous sinus, and where the resulting paralysis appears in the distribution of the third and sixth nerves. But by extension of the thrombosis into, say, the petrosal sinuses, nerves other than the two just mentioned may also be implicated, and in this way a comparatively wide area of paralysis may be produced, presumably by the pressure of blood clot. Again, thrombosis must be considered in connection with the

disturbances likely to occur in the tissues in the immediate neighbourhood of the obstructed vessel. These disturbances include such events as hæmorrhage, œdema, and softening, any one of which, if favourably situated, may readily interfere with the functions of the centre or trunk of one or other of the cranial nerves. Possibly such considerations, though plainly applying to ocular paralyses occurring in anæmia, may be said to leave untouched the issue in regard to optic neuritis. Yet even here the chance of finding an explanation is not altogether hopeless. A thrombus, particularly if it is formed in one of the larger sinuses, may be regarded as a "foreign body" or "adventitious product" within the skull, and in this sense comes under Hughlings Jackson's definition of intra-cranial tumour. So presented it appears as a not improbable cause of optic neuritis, or at least the connection between it and optic neuritis is hardly more mysterious than is the connection between optic neuritis and any other form of "tumour." With this suggestion, too, must be taken the fact that sinus thrombosis pure and simple is very much less likely to be accompanied by general symptoms of cerebral disturbance than is thrombosis affecting the cerebral veins. Indeed, there can be little doubt that a limited sinus thrombosis may occur entirely without clinical evidence of the fact. On the other hand, it is in cases where the cerebral veins are involved—and especially where they are extensively involved—in the thrombotic process, that severe and general symptoms display themselves. Hence there is no difficulty in imagining in a case of anæmia a sinus thrombosis sufficient to cause such a limited clinical expression as optic neuritis and yet failing, in consequence of non-extension of clot formation to the cerebral veins, to excite any general exhibition of cerebral disturbance. Such a suggestion, it may be held, provides a possible explanation of optic neuritis appearing as an isolated event in anæmia, and also meets the objection that, were the cause of such neuritis thrombus formation within the skull, there must needs be clinical evidence of this on a more or less extensive scale. In any event, whether the proposals here advanced on the theoretical aspects of optic neuritis and ocular paralyses occurring as clinical facts in cases of anæmia are, or are not, warranted, it is beyond question that intra-cranial thromboses may and do occur in anæmia, and that among the clinical evidences of such thromboses optic neuritis and ocular paralyses are most unquestionably to be numbered.

Again, it has been urged that if thrombosis of the veins and sinuses within the skull can cause optic neuritis the same

result ought to follow blocking, as by thrombosis or embolism, of the cerebral arteries, and this admittedly (unless the clot be septic) is not the case. With all deference, the relevance of this argument may be contested. The circulatory and other changes which follow obstruction of an artery are not identical with those produced by obstruction of a vein, and in view of the admitted obscurity of the relations between optic neuritis on the one hand and intracranial lesions on the other, it is hardly safe to conclude that because arterial thrombosis does not cause optic neuritis venous thrombosis must necessarily fail to do so. Against such a conclusion, further, may be set the facts of experience, which compel the conviction that between venous thrombosis and arterial thrombosis there is, so far as optic neuritis is concerned, some essential difference. The one, whatever be the explanation, is, or may be, in the clinical order of events associated with optic neuritis, and the other has no such association. In view of such facts it seems idle to argue that because arterial obstruction does not cause optic neuritis venous obstruction must also be incompetent in this respect. The facts show the contrary. *Hippocrate dira ce qu'il lui plaira; mais le cocher est mort.*

Once more, it has been said that whereas the optic neuritis of anæmia commonly subsides as the anæmia disappears under the administration of iron, this fact shows that the neuritis is due to some depreciation in the quality of the blood; were the neuritis due to thrombosis the therapeutic use of iron could not have any effect on it. The answer to this is that the optic neuritis of anæmia, even when iron is prescribed, by no means always disappears promptly, and that its movement is far from keeping strict time with the improvement in the blood quality. On the contrary, it may persist for weeks or sometimes even for months after all the ordinary evidences of anæmia have completely disappeared. Further, it must be accepted that optic neuritis—and the same is true of the evidences of thrombosis generally—is not confined to cases in which the degree of anæmia is extreme. It may, indeed, exist with but moderate evidences of anæmia, and is frequently absent in the more severe cases—facts difficult to reconcile with the view that it is due directly to some blood defect. On the other hand, the suggestion of thrombus formation and persistence is readily consistent with an optic neuritis which endures in spite of a cure of the anæmia, while ultimate disappearance of the neuritis may reasonably be attributed to removal of the

thrombus by those natural processes under the operation of which the channel of a thrombosed vessel may be completely restored.

Thus, to summarise the objections, it may be said that neither a difficulty in providing a manifest explanation of the mechanism by which sinus thrombosis may produce optic neuritis; nor the claim that the frequent absence of evidence of general cerebral disturbance with such neuritis opposes the diagnosis of intracranial thrombosis; nor the observation that in arterial thrombosis optic neuritis does not occur; nor the comment that the neuritis disappears under treatment by iron—is found, on examination, to present any insuperable objection to the proposition that optic neuritis occurring in anæmia has, in all probability, its explanation in the formation of blood clot in the veins or sinuses of the brain.

Attention may now be directed to certain other hypotheses which have been advanced to explain the occasional existence of optic neuritis in anæmia. One of these suggests that the cases are really examples of poisoning either by lead or syphilis and that to one or other of these agents both the anæmia and the neuritis must be attributed. It may be said at once that there is little, if any, positive evidence to support this statement. The recorded cases do not exhibit any of the usual symptoms of plumbism or syphilis, and the cure is effected, not by remedies appropriate to these diseases, but by the direct treatment of the anæmia. It may also be remarked that optic neuritis as it occurs in anæmia is frequently marked by very considerable swelling of the optic discs, and is on this account much more suggestive of some definite intracranial lesion than of a toxic condition of the blood, in which, when it produces optic neuritis, the swelling of the discs is a comparatively insignificant fact. Indeed, the ophthalmoscopic picture in the optic neuritis of anæmia often exactly agrees with the facts common in intracranial tumour, and unless this is remembered a serious error in diagnosis may be made, especially if, as is not uncommon in anæmic women, the patient also suffers from more or less severe headache and from occasional attacks of vomiting. (Gowers.)

According to a second theory, the optic neuritis of anæmia depends on œdema of the brain. This, however, is little more than an empty phrase. The only evidence in support of such a view is, perhaps, to be found in some few cases in which the existence of optic neuritis in association with amenorrhœa has

been recorded, the necropsy revealing an excess of fluid in the cerebral ventricles. Such a pathological condition can, however, hardly have been a primary one, and in the absence of any definite statement in reference to thrombosis it seems not unlikely that the cases were really cases of anæmia, and that the essential intracranial change was clot formation in the cerebral veins and sinuses—a condition which, unless special search is made for it, may be readily overlooked even on *post-mortem* examination.

Demanding more respect than either of the foregoing suggestions is the view advanced by Sir William Gowers—namely, that optic neuritis in chlorosis depends partly on continued congestion of the optic discs due to hypermetropia, and partly on a toxic or other abnormal quality of the blood. On this, with great deference, it may be remarked that hypermetropia is not present in all cases of chlorotic optic neuritis, and that in any event it is difficult to believe that eye-strain, even when acting in co-operation with some deleterious agent present in the blood, can explain the extreme degree of swelling of the optic discs which has repeatedly attracted attention in the cases now under consideration. Further, neither eye-strain nor toxæmia will readily account for a unilateral ocular paralysis, which, as has already been shown, occasionally accompanies the optic neuritis of anæmic women. Hence, in such a case, it is necessary, on the view now under discussion, either to invoke two separate and distinct causes—one for the optic neuritis and a second for the ocular paralysis—or to argue that optic neuritis accompanied by an ocular paralysis in a case of chlorosis owns a different cause from the one in operation when, in similar conditions, optic neuritis appears apart from such paralysis. It may be fairly said that neither of these alternatives offers an inviting choice. On the other hand, thrombosis, which, in the circumstances, must be admitted as at least a possibility, is adequate to explain all the facts—both the optic neuritis and ocular paralysis existing in association and the optic neuritis present as an isolated event. In short, while any theory other than intracranial thrombosis interposes a gap between cases of chlorosis accompanied merely by optic neuritis, and cases of the same disease in which there exist together with optic neuritis various other evidences of cerebral disturbance, thrombosis brings all these cases into a common category, and, while recognising a wide variety in the extent and severity of the clinical manifestations, includes all alike in an identical order.

Turning now from optic neuritis and ocular paralyses as occasional events in the clinical history of simple anæmia, attention may next be directed to certain disturbances of the visual fields which may exceptionally appear as complications in this disease. Probably these are very rare, and it is to the courtesy of my hospital colleagues that I am indebted for the opportunity of studying the two instances which have come under my observation.

The first[1] was that of a woman, aged 34 years, in whom there was detected a right homonymous hemianopsia (Fig. 1). This condition had been present for thirteen years, as was proved by perimeter charts in the possession of the patient and taken near the date of onset. At that time she was, to use her own words, suffering from "dyspepsia and bloodlessness," and was being treated as an out-patient at a London hospital. Suddenly, one morning, when engaged in her occupation as a tailoress, she had an attack of "dizziness," and noticed that as she carried her hand to the right, as in the act of stitching, it disappeared from view, and that generally she was unable to see objects situated to her right side—a state of matters which still persists. Yet, with this exception, she has continued to enjoy fair health, and certainly has been, and still is, entirely free from all symptoms of active intracranial disease. The occurrence of the hemianopsia, it will be allowed, involves the existence of some cerebral lesion, and the sudden development of this symptom suggests most strongly that the lesion was of circulatory origin. The youth of the patient, 21 years, other facts apart, may be taken as sufficient to exclude hæmorrhage. In these circumstances thrombosis inevitably suggests itself, and the relatively "quiet" character of the seizure favours such a view. Even if a diagnosis of embolism be preferred the absence of cardiac valve disease makes it necessary to allow thrombus formation either in the heart itself or somewhere in the arterial system on the proximal side of the obstructed vessel. Hence, on either diagnosis, the case may be quoted to illustrate one aspect of the possible range of thrombosis in cases of anæmia. On the whole, the probabilities may be claimed as favouring venous thrombosis, and if this is accepted, the case enforces a view already advanced—namely, that such thrombosis may cause a limited, though definite, clinical expression without at the same time producing anything like widespread evidences of cerebral disturbance.

[1] Mr. W. Ilbert Hancock's case; reported in detail in *Practitioner*, December, 1904.

FIG. 1.

Right homonymous hemianopsia in a woman of 34 years. Onset sudden when patient suffering from "dyspepsia and bloodlessness" at 19 years of age. *(Reproduced by permission from the "Practitioner.")*

A second case,[1] claimed to belong to the same order, is that of a woman, aged 32 years, who has been under observation during the last few years, and who, save for the facts now to be mentioned, is free from all evidence of organic disease. Her original complaint was of breathlessness and scanty menstruation, and she was found to be the subject of a moderately severe anæmia. Without any other disturbance she suddenly became aware that, as she put it, "I could not see round about me." The visual charts were taken, and a decided contraction of each visual field, but more particularly of the right field, was detected (Fig. 2). Otherwise there was no evidence of intracranial disease, and the general clinical examination of the patient, except for the fact of anæmia, was entirely negative. Gradually, in the following weeks, the fields moved towards their normal limits, but even yet there is absence of peripheral vision in the upper nasal quadrant of the right field, and this, in view of the lapse of time, must probably be accepted as a permanent defect. Here again is a limited cerebral disturbance occurring suddenly in a woman free from all evidence of disease other than anæmia. In the circumstances the suggestion of thrombosis in the higher reaches of the central visual nervous apparatus on the left side can hardly be resisted. Even if it is objected that the initial bilateral character of the visual disturbance necessitates a bilateral lesion, the argument in regard to thrombosis is not appreciably weakened. And further, it may be answered that a bilateral lesion as an explanation of the visual disturbances is by no means necessary. When it is remembered that in functional hemiplegia, where, presumably, the central disturbance is confined to one hemisphere, contraction of the visual field, though most marked in the eye opposite to the inactive hemisphere, may be detected also, at least in some measure, in the eye of the same side, it is not difficult to accept an area of thrombosis limited to the hinder part of the left parietal lobe as the explanation both of a temporary limitation of the periphery of both visual fields and also of a permanent defect confined to the field of the right eye. This is the suggestion here submitted as the interpretation of the present case, and the record is offered as a further illustration of the range of intracranial thrombosis as this occurs in cases of anæmia.

I next submit retinal embolism as an event of occasional occurrence in anæmia and demanding thrombosis as its

[1] Mr. T. Brittin Archer's case.

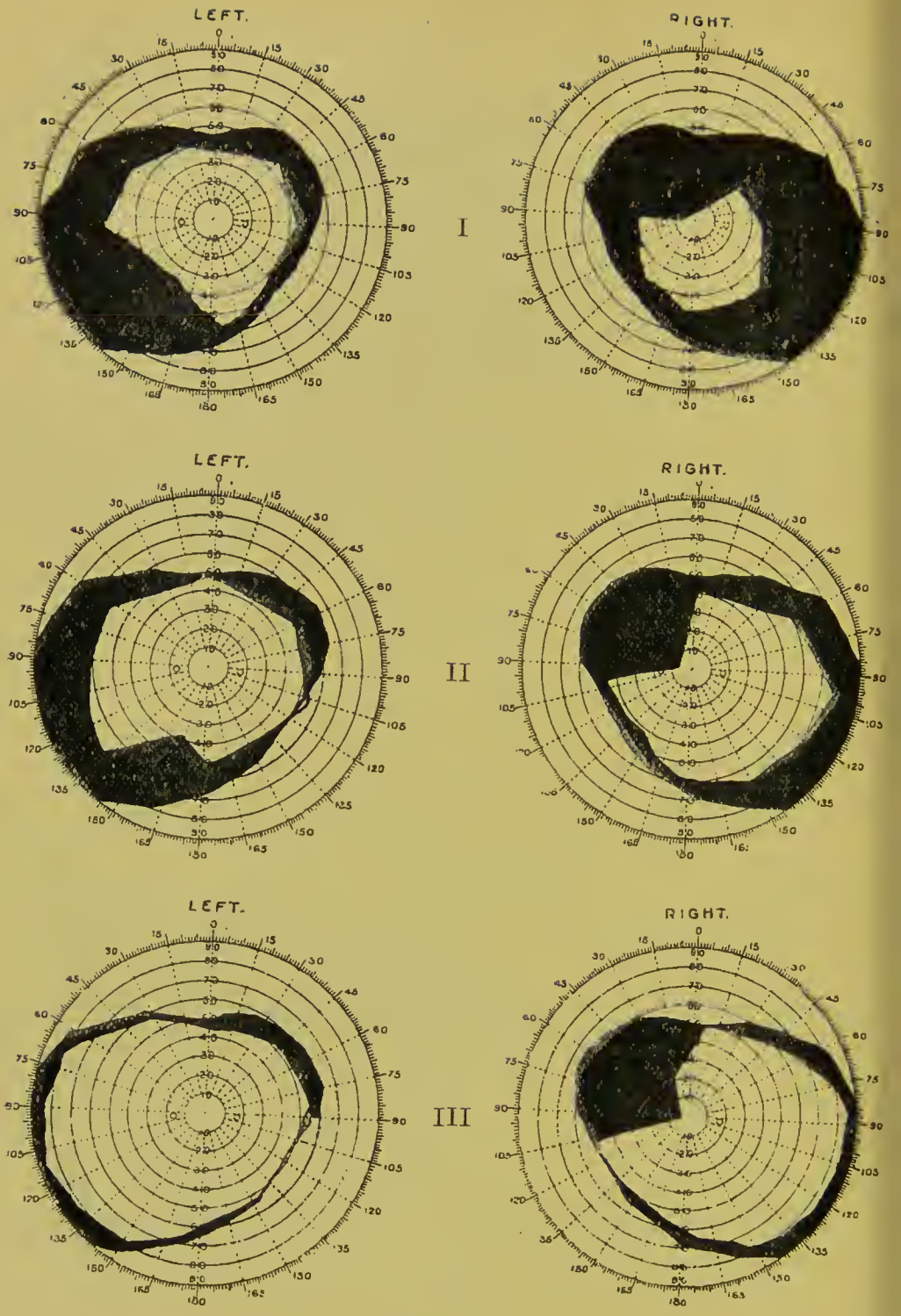

FIG. 2.

I, Charts taken in May, 1904; II, charts taken in August, 1904; III, charts taken in July, 1905, and confirmed on several later dates. From the case described in text, p. 17.

interpretation. In my own note-books I find records of three cases of embolism in which no abnormal fact other than anæmia could be detected. The patients were females, aged 21, 27, and 42 years. In none of the cases was there a history of rheumatism, and all alike were free from evidences of cardiac disease and of arterial degeneration. That the central artery of the retina was in each instance blocked there could be no doubt. For this, in the absence of cardiac valve disease, no obvious explanation could be found. Yet from the existence either of embolism or of thrombosis *in situ* it was, in view of the fact of arterial obstruction, impossible to escape. Opinions may possibly differ as to which of these two is in the circumstances the more probable, but either involves the admission of clot formation in one or other part of the cardio-arterial system, and this must apparently be attributed to the anæmia. It seems reasonable to suggest that the primary clotting took place in one or other of the two chambers of the left heart and that the cases were therefore true examples of retinal embolism. In some of the fatal cases of chlorosis attended with intra-cranial venous thrombosis the presence of intracardiac thrombi has been observed, and thus the suggestion here proposed has a certain basis of actual anatomical observation in its favour. It is also true that primary arterial thrombosis has in a few exceptional cases of anæmia likewise been recorded, and therefore this alternative explanation of the cases now under discussion must be admitted as possible. But either view serves the present argument—that obstruction of the retinal artery must be included among the complications which arise in anæmia as a result of the tendency in that condition to the formation of intravascular blood-clot.

Lastly, as an occasional complication in anæmia, and possibly due to thrombosis, may be mentioned retro-bulbar neuritis. This, in its typical form, is characterised by sudden loss of central vision in one eye without evident ophthalmoscopic change, although at a later date there may be whitening of the disc, due presumably to some measure of optic nerve atrophy. These facts demand a lesion in the trunk of the optic nerve posterior to the eyeball, and the suddenness of the event often suggests that the lesion is vascular in nature. It may, therefore, be thrombosis, and the fact that complete recovery may occur is manifestly in entire harmony with this conclusion. No doubt retro-bulbar neuritis is also seen in

conditions other than anæmia, but this does not qualify the experience that it is occasionally met with in patients free from all evidences of disease except anæmia (Fig. 3). Nor does it negative the suggestion that the proximate cause of the condition, whether when associated with anæmia, or otherwise, may be thrombosis. It is no doubt true that retro-bulbar neuritis is sometimes an event in the evolution of disseminated sclerosis. But most certainly it exists apart from this disease.

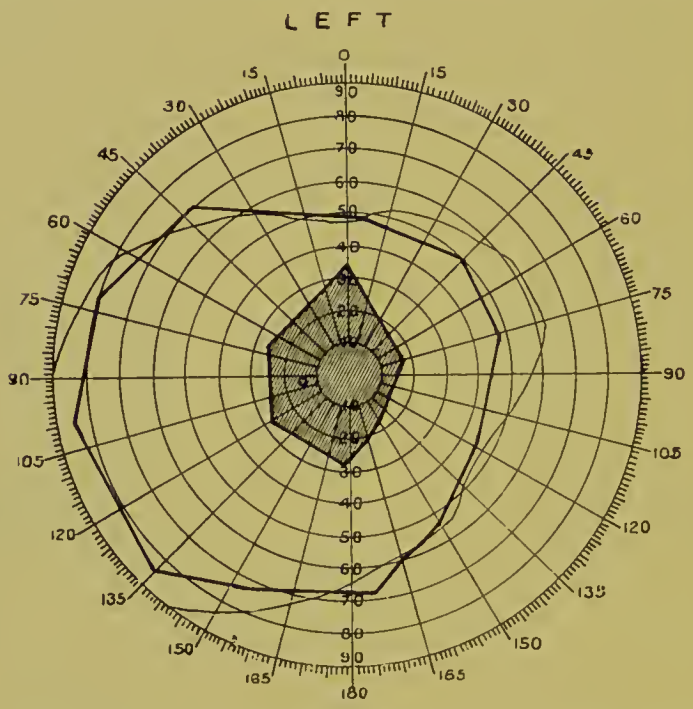

FIG. 3.

Central scotoma from retro-bulbar neuritis in a case of anæmia. Central vision was restored in about six weeks, and patient, when seen three years later, was free from all evidences of disease.

Indeed, it occurs in patients in whom clinical observation, even when extended over a term of years, fails to detect any evidence of organic disease, and some of these are anæmic women, that is, are patients in whom thrombosis is a well-recognised possibility. Thus there seem to be reasons to accept the view that while some ocular complications in anæmia may be due to thrombosis of the intracranial veins and sinuses, others may depend upon thrombosis in the vessels, probably the veins, of the peripheral visual apparatus, and

among these latter may be placed retro-bulbar neuritis. But the possibility of a peripheral thrombosis cannot be limited to cases coming typically under this diagnosis. The fact is that the unilateral ocular complications of anæmia range from a greater or less degree of papillitis without prejudice to vision, to a condition of complete loss of visual acuity with little or no ophthalmoscopic change. And between these two extremes there are intermediate cases which show in varying proportions, as it were, some measure both of papillitis and of visual defect. Assuming thrombosis as responsible for these facts, it is readily conceivable that the several varieties and combinations may be determined by the particular site at which the formation of blood-clot takes place. Should this occur at or near the optic disc it may well produce exudation and hæmorrhages of a more or less serious character upon and around the disc—a papillitis in short; and with such a condition, as is common knowledge, there is no necessary decline of visual acuity. On the other hand, should thrombosis affect vessels in the trunk of the optic nerve behind the eyeball serious interference with vision, and especially with central vision, will be a prominent symptom, although, at least in the early stages of such a case, the fundus may appear normal or may show nothing more than some fulness of the retinal veins. In the intermediate cases, that is those in which papillitis and visual defect are both present, it may be surmised that thrombosis has involved vessels both on or near the optic disc and also those of the nerve trunk. One further remark in connection with these cases may be added—it does sometimes happen that a patient shows papillitis in each eye and in one or both eyes also a serious reduction of visual acuity. The latter fact, as already suggested, implies a lesion in the optic nerve trunk. Therefore when with double papillitis there is marked visual loss it seems probable that the thrombosis, assuming this to be the responsible lesion, is bilateral and peripheral, and further warrant for this view may be found in cases described as retro-bulbar neuritis in which the affection attacks both eyes, either simultaneously or in rapid succession. Thus there may be distinguished in anæmia two groups of cases in which bilateral papillitis (optic neuritis) is present. In one there is marked visual defect, and here, for reasons just given, the probabilities are in favour of a bilateral peripheral lesion. In the other and more common variety there is little or no impairment of vision. In such circumstances it is sufficient to assume, as has already been

suggested, a central or intracranial thrombosis, and the experience that with this order of neuritis more or less conspicuous clinical evidences of cerebral disturbance are sometimes present may be advanced in support of such an assumption. But in both groups, as well as in other cases in which optic neuritis and visual loss, either alone, or in combination, are present, it may be submitted that thrombosis affords a possible explanation of the facts, and that by such explanation these cases are brought into a reasonable relationship with other cerebral and ocular conditions which occasionally manifest themselves in patients in whom, in spite of exact and continued clinical observation, nothing abnormal can be discovered other than a depreciated quality of the blood.

Such then, in outline, are some of the cerebral and ocular complications[1] which may appear in the subjects of simple anæmia. It may perhaps be said that these accidents are very unusual. Still, they occur, and therefore demand explanation; and it is possible that in their slighter forms they would more frequently be discovered were examination made for them. Further, the infrequency of these complications is by no means out of harmony with the suggestion that they depend on thrombosis; as, however it may be explained, thrombosis, although a potential development in all cases of anæmia, only in rare instances takes shape and form as a definite clinical occurrence. If the view here advocated is accepted, the occasions of thrombosis are somewhat enlarged, but even so increased there is no desire to pretend that these occasions are either relatively or absolutely frequent. Whether few or many, however, it is to be desired that clinical events shall be duly arranged in their appropriate order and relationship. The hypothesis here advanced is an attempt in this direction. Assuming it to be justified, it brings under a common explanation a number of events which, apart from it, are isolated and detached alike from one another and from the state of anæmia to which, in some fashion or other, their existence is undoubtedly due. In the practical sphere, the suggestion that optic neuritis, ocular paralyses,

[1] Hæmorrhages in the retina are occasionally seen in patients suffering from chlorosis and may possibly be either direct or secondary to thrombosis. They are quite exceptional, and even when present probably not more than one or two will be detected. In pernicious anæmia, on the other hand, multiple retinal hæmorrhages are the rule.

hemianopsia or other abnormalities of the visual field, retinal embolism, and retro-bulbar neuritis, occurring in anæmic patients, are probably due to thrombosis, is significant, because on such interpretation any one or more of these events appearing in an individual case must be accepted as the sign of a tendency to thrombosis in an unusually marked degree, and must therefore claim the prompt and appropriate therapeutic measures which such a conclusion demands.